Functional Colonoscopy using Dark Lumen DCE-MRI

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Introduction: The *Min* mouse represents an appropriate model for the study of early-stage colon tumor progression as a result of its similarity in genotype and phenotype to the human Familial Adenomatous Polyposis coli (FAP) syndrome that predisposes to colon cancer. The non-invasive serial evaluation of these spontaneously arising tumors presents special challenges for MRI given the tortuous nature of the intestines and the relatively small size of the polyps (≤ 3mm). Dark lumen-based colonoscopy has demonstrated reasonable success in detecting experimental and clinical colon polyps (1,2). Dark lumen MRI relies on minimizing the signal intensity of the intestinal lumen and reducing susceptibility artifacts while enhancing the signal from the lumen wall and any masses using intravenous injections of paramagnetic contrast agents. The purpose of this study is to develop a new approach to eliminate the lumen signal intensity while improving polyp detectability and also to evaluate the potential of dynamic contrast enhanced (DCE) MRI to characterize the polyp microenvironment.

Methods: We have currently performed dark lumen MRI on 5 untreated and 1 dextran sodium sulfate (DSS) treated (a promoter of polyp growth) *Min* mice using a Varian 7T scanner. Prior to imaging, fecal matter was removed from the colon by rectal enema. To eliminate the lumen signal the colon was back-filled with a perfluorinated oil (containing no hydrogen) and the anus was sutured. A high-resolution 2D GRE scout scan (TR/TE/α = 1000 ms/3 ms/20°, 30 slices, ST = 0.5 mm FOV = 60 mm x 40 mm, matrix = 256 x 256, NEX = 4) was initially performed to identify polyps and for slice selection for the DCE-MRI study. We also performed a slab selective 3D GRE sequence (TR/TE/α = 15 ms/4.85 ms/20°, NEX=4, FOV = 60 mm x 40 mm x 40 mm, matrix = 256 x 128 x 128) to collect the images that are used to render the virtual colonoscopy. A variable flip angle spoiled GRE approach (TR/TE = 400 ms/4.85 ms, α = 12°, 24°, 36°, 48°, 60°, FOV = 60 mm x 40 mm, matrix = 128 x 128, NEX = 4, 5 slices, ST = 0.5 mm) was employed to produce T1-maps. The DCE-MRI protocol was implemented in 3 of the 6 studies and employed a similar GRE sequence (TR/TE/α = 400 ms/4.85 ms/36, NEX = 2) to obtain 35 serial images following an intravenous injection of Gd-DTPA. The dynamic images were registered to the T_1-map using a rigid registration technique preferentially weighted to each polyp. Since peristalsis prevented a voxel-wise analysis of the DCE-MRI time series, we averaged the signal intensity over a polyp ROI and applied the reference region model to calculate K^{trans} and v_e (3). The 3D images were used to quantify the polyp volume and dimensions.

Results: Distending the colon with oil virtually eliminated the lumen signal, and allowed the identification of all parts of the rectum and colon from the anus to the cecum. Figure 1 shows a sample image selected from a 3D GRE dataset. Three polyps are clearly visible in this slice (largest dimension of each ~ 3mm). The mean polyp volume and largest dimension for the 5 untreated mice (16 polyps) was 6.3 mm^3 and 3.2 mm, respectively. For the 1 DSS treated mouse (3 polyps) the mean volume and largest dimension was 22.45 mm^3 and 3.9 mm, respectively. Out of all the mice, the largest dimension of the *smallest* polyp detected (volume = 0.69 mm^3) thus far was 1 mm. This same polyp grew to a volume of 1.79 mm^3 (largest dimension = 1.5 mm) after 7 days additional growth as measured in a subsequent MRI study. Figure 2 shows examples of the mean concentration time curves (# voxels) in muscle and polyp (the most anterior polyp in Fig. 1) ROIs acquired using DCE-MRI. With our current registration algorithm, polyp registration of the dynamic time series has been most successful with polyps located in the descending colon (like those in Fig. 1). The mean K^{trans} and v_e for 2 untreated polyps was 0.35 min^{-1} and 0.29, respectively.

Figure 1

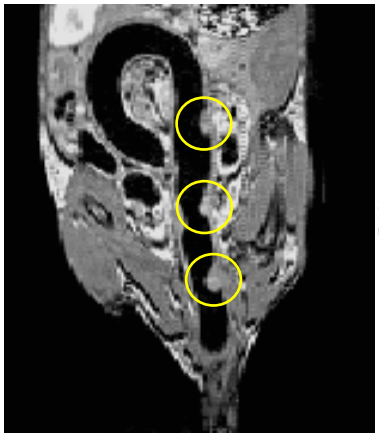
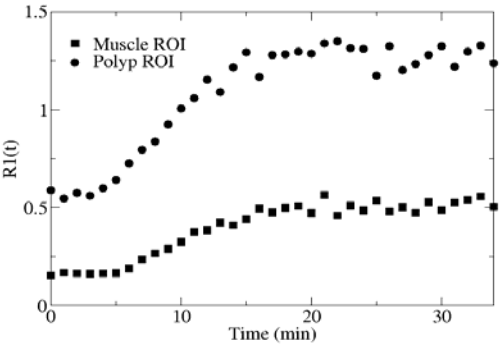


Figure 2



Discussion: These preliminary studies have demonstrated that dark lumen imaging using oil as a back-filling agent enhances the delineation of the colon and polyps. We are currently validating the accuracy of this approach by quantifying the tumor volume in *ex vivo* studies. This is also the first study to evaluate a polyp's physiological microenvironment using DCE-MRI. By improving the registration techniques and utilizing spasmolytic agents we plan to improve the applicability of the DCE-MRI approach throughout all segments of the colon. We are also developing similar dark lumen MRI methods to study small intestine adenomas. Combining these two methods will provide a comprehensive approach to monitor intestinal carcinogenesis and treatment response *in vivo*.

References: Hensley HH, *et al*. Mag Reson Med 2004; 52:524-529. 2. Burcu N, *et al*. Eur Radiol 2004; 14:1535-1542.
3. Yankeelov T, *et al*. Mag Res Imag 2005; 23: 519-529.